1. Introduction

Neurodegenerative diseases are a growing public health concern. Early detection and monitoring of disease progression are crucial for developing effective interventions. Serial magnetic resonance imaging (MRI) offers a unique advantage by enabling the longitudinal assessment of whole-brain volume changes. This quantitative approach can provide insight into the rate of cell atrophy. In this study, we examine changes in whole brain volume at two time points using serial MRI in a sample categorized into three groups: dementia, no dementia, and those who converted to dementia over time. We hypothesize a significant differences in normalized brain volume between dementia group (dementia, no dementia, converted); however, it is unclear whether this relationship may change across time points. *A priori*, we would expect the dementia and converted groups to exhibit a greater rate of decrease (nerodegeneration) in whole-brain volume across the two time points compared to the no dementia group.

2. Dataset

The dataset comprises longitudinal MRI data obtained from a cohort of older adults aged 60 to 96, and measures changes in brain volume over time. The brain volumes were normalized for total intracranial volume. The study initially included participants with multiple visits; however, to ensure balanced sample sizes across the two-time points, six participants with only one visit were excluded from the analysis, resulting in a total of $N = 144$ participants with scans from two visits.

3.1 Mixed Measures ANOVA Model 1

Research Question for Model 1: Do changes in normalized brain volume across time points differ between the three diagnostic groups (dementia, no dementia, and converted to dementia over time)?

We employed a mixed-measures analysis of variance (ANOVA) using the pingouin library in Python to investigate the effects of time and diagnostic group on brain volume. Brain volume was considered the dependent variable. Time (baseline vs. follow-up scan) served as the within-subjects factor, while diagnostic group (dementia, no dementia, converted) acted as the between-subjects factor. The ANOVA results will assess the main effects of time and group, as well as the interaction effect between time and group. First, we check for several assumptions underlying mixed measures ANOVA's in our data set.

3.1.1 Assumption Checking

✓ Normality: brain volume for each condition are sampled from a normally distributed population.

Group	Shapiro-W	p-value	normal
Nondemented	0.989	0.306	True
Demented	0.991	0.576	True
Converted	0.957	0.386	True

Table 1. Shapiro-Wilke Test of Normality for Diagnostic Groups

Homogeneity of variance: each population should have the same error variance. Levene's test statistic is calculated across diagnostic groups (*Levene's* = 0.89, p = 0.41)

✓ **Sphericity of the covariance matrix.** Mauchly's test of sphericity is used to check for this assumption ($p > .05$). Since Time has only two levels (Pre and Post), the sphericity assumption is necessarily met.

✓ **Quantitive Variables:** The dependent variable (normalized brain volume) is continuous.

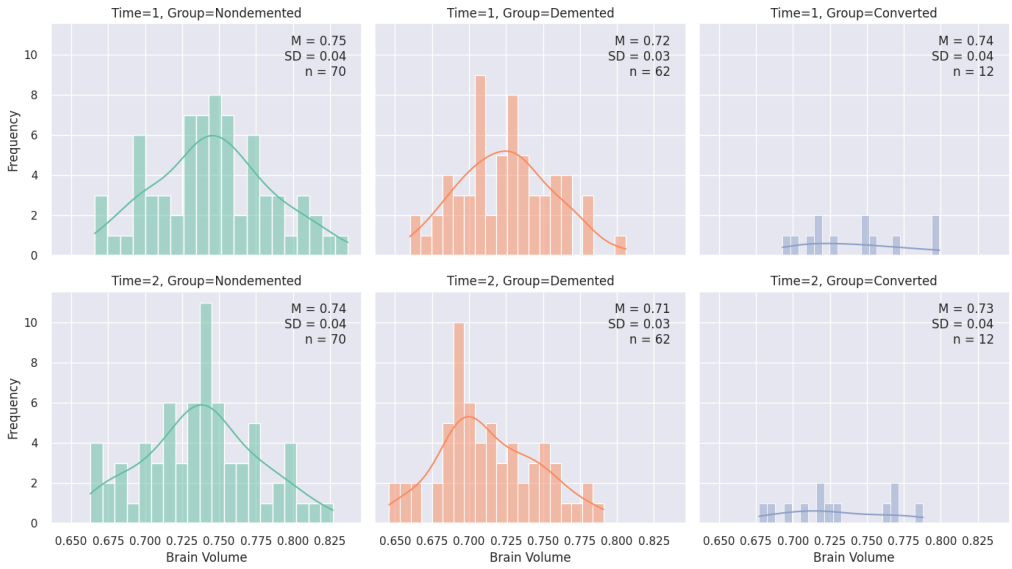

Figure 1. Distribution across Diagnostic Groups and Time

3.1.2 Interaction Plot and Inferential Statistics

Source	SS	DF1	DF2	MS	F	p-unc	np2
Group	0.03	2	141	0.02	6.71	0.00	0.09
Time	0.01	1	141	0.01	94.25	0.00	0.40
Interaction	0.00	2	141	0.00	1.53	0.22	0.02

Table 2. Mixed Measure ANOVA Results: Model 1

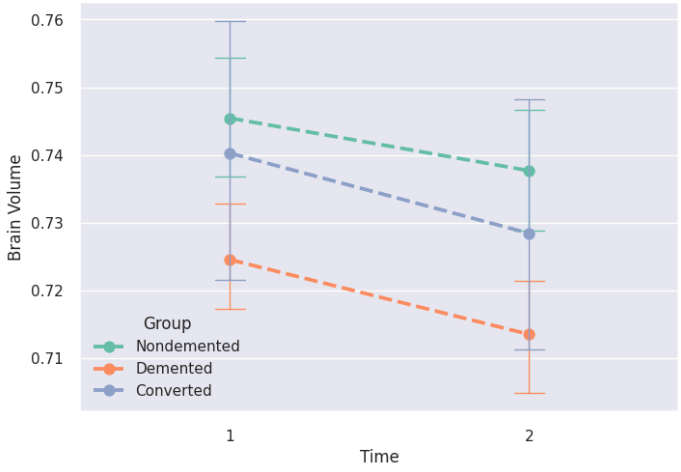

Figure 2. Interaction Plot for Brain Volume over Diagnostic Group and Time

3.1.3 Post-Hoc Tests

Contrast	Time	A	B	T	dof	p-unc
Time	-	1	2	9.67	143.00	0.000
Group	-	Demented	Nondemented	-3.69	129.43	0.000
Time * Group	1	Demented	Nondemented	-3.41	129.01	0.001

Time * Group	2	Demented	Nondemented	-3.86	129.95	0.000

Table 3. Significant Post Hoc Results for Model 1

3.2 Mixed Measures ANOVA Model 2

Research Question for Model 2: Do changes in normalized brain volume across time points differ between men and women with dementia?

In the second repeated measures ANOVA model, we examine whether there are significant differences in the mean normalized brain volume (dependent variable) across the two-time points (within-subjects) for men and women (between-subjects factor) for the demented diagnostic group only; here, we question whether men and women with dementia experience different rates of atrophy, controlling for variation accounted for by brain volume at time point one (pre-diagnosis).

3.1.1 Assumption Checking

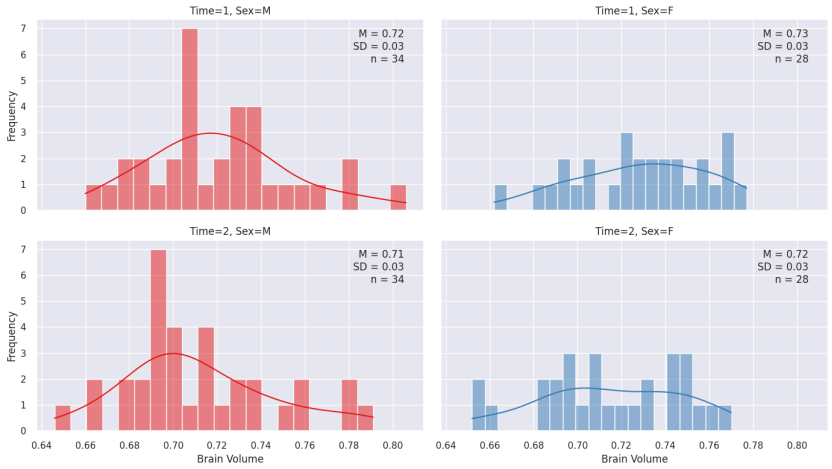

Figure 3. Distribution across Sex and Time for Demented Older Adults

✓ **Homogeneity of variance:** Levene's test statistic is calculated across sex (*Levene's* = 0.01, p = 0.91)

✗ **Normality**: brain volumes for each sex are not sampled from normally distributed populations. Violation of this assumption may inflate the type I error rate.

M/F	Shapiro's W	p-value	normal
M	0.969	0.007	False
F	0.992	0.440	True

Table 4. Shapiro-Wilke Test of Normality for Males/Females with Dementia

3.2.2 Interaction Plot and Inferential Statistics

Figure 4.

Source	MS	F	p-value	np2
M/F (With Dementia)	0.001	0.431	0.514	0.007
Time	0.004	41.898	0.000	0.411
Interaction	0.000	1.985	0.164	0.032

Table 5. Mixed Measure ANOVA Results: Model 2

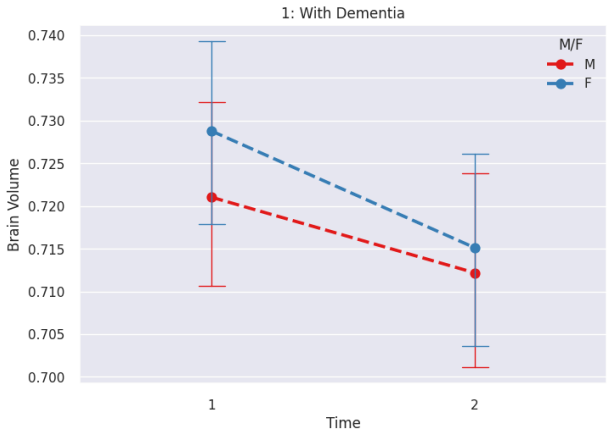

Figure 4. Interaction Plot for Brain Volume over Sex and Time for Demented Group

4.0 Results and Discussion

This study investigated changes in normalized brain volume across time points using mixed-level ANOVAs. Both models (diagnostic groups and gender within dementia) revealed a significant main effect of time ($p < 0.05$). This indicates that brain volume declined on average across the measured time points, regardless of diagnostic group or participant gender within the dementia group. For the diagnostic group model, a significant main effect was also found between the demented and non-demented groups ($p < 0.05$). This suggests a difference in average brain volume between individuals with and without dementia. However, the interaction effect between time and diagnostic group was not statistically significant ($p > 0.05$)– the rate of brain volume change over time did not differ significantly between the groups. The gender model within dementia showed no significant difference in brain volume between men and women ($p > 0.05$). Interestingly, an emerging but non-significant interaction effect between time and gender was observed. This effect warrants further investigation to determine if the rate of brain volume change differs subtly between genders within the dementia population.

Limitations

- Did not control for temporal effects of differences in delay time between scans
- No controlling for Age
- Violation of normality in comparison across sexes

Power Curve

Power curves for varying effect sizes in an independent t-test at alpha =.05. To achieve 0.91 power with a 0.7 effect size, a sample size of 46 is needed.